

### **REMARKS**

Upon entry of this amendment, claim 43 is canceled without prejudice or disclaimer, claim 51 is added, and claims 22, and 44-46 are amended.

#### **Rejections Under 35 USC § 112, ¶ 1**

Claim 22 has been amended to recite that the derivatives of the parathyroid hormone (“PTH”) are peptide fragments of PTH. Peptide fragments of the PTH do not include fragments that are not structurally related to PTH, thus only fragments that are related to PTH are claimed. Accordingly, the Examiner’s rejection to claim 22 on the ground that it includes “any and all conceivable compounds, including those that are structurally unrelated to PTH,” has been rendered moot.

#### **Rejections Under 35 USC § 102**

Applicants traverse the rejection of claim 22 for anticipation over Kamata and Davidovitch, respectively. As explained below, the present invention is clearly different from what either Kamata or Davidovitch teaches.

Applicants have amended claim 22 to recite continuous administration. The Examiner misinterprets the meaning of continuous in alleging that the daily administration of Kamata or Davidovitch is continuous. As highlighted in Example 2, *inter alia*, the daily administration of Kamata or Davidovitch was not continuous but intermittent. That is, Example 2 compares intermittent administration (daily injection) to continuous administration. By contrast, the continuous administration was a sustained release dosage from an implanted osmotic pump.

Moreover, Kamata only describes the administration of parathyroid extract to parathyroidectomized rats only, with no implication relevant to administration of PTH or a PTH derivative to non-parathyroidectomized patients.

**Rejections Under 35 USC § 103**

Claims 22, 49, and 50 stand rejected over Gianelly in view of Kronenberg, Gardella and Sindrey or Davidovitch and Schluter. Applicants traverse this rejection on the grounds that the Examiner has failed to establish a *prima facie* case of obviousness.

Claim 22, the independent claim directed to the present invention, recites “administering continuously” rather than a single, daily injection. No permutation of the cited references reasonably suggests that a continuous administration could result in an increase in tooth movement.

Moreover, no combination of these references would have prompted one of ordinary skill to expect the demonstrably superior results of the present invention. The examples of the present specification teach that tooth movement by continuous PTH infusion is significantly promoted as compared with that by intermittent PTH injection. For example, see page 21, lines 2-13, and Figure 10. In the case of local injection, sustained release PTH exhibits a superior effect than intermittent PTH injection. See page 21, lines 14-28, and Figure 11, *inter alia*.

At the time of filing the present application, furthermore, it was unknown that the action of PTH by continuous infusion might be different from that by single or intermittent injection. Accordingly, the skilled artisan would not have been able to extrapolate the results of intermittent administration to those of continuous administration. See Dempster *et al.* (Exhibit 1), at 696-697, Dobnig and Turner (Exhibit 2), at 4609-4610, and Moseklide and Reeve (Exhibit 3), at 1298.

**Rejections Under 35 USC § 112, ¶ 2**

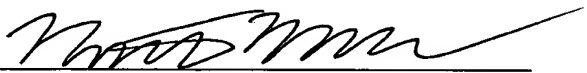
Claim 43 has been cancelled, rendering this rejection moot.

**Conclusion**

In view of the foregoing amendments and remarks, applicants respectfully submit that all of the pending claims are now in condition for allowance. An early notice to this effect is earnestly solicited. If there are any questions regarding the application, the Examiner is invited to contact the undersigned at the number below.

Respectfully submitted,

Date October 31, 2002

By 

FOLEY & LARDNER  
Washington Harbour  
3000 K Street, N.W., Suite 500  
Washington, D.C. 20007-5143  
Telephone: (202) 672-5300  
Facsimile: (202) 672-5399

Matthew E. Mulkeen  
Agent for Applicants  
Registration No. 44,250

**Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees; and applicant(s) hereby petition for any needed extension of time.**

## MARKED UP VERSION SHOWING CHANGES MADE

### IN THE SPECIFICATION

This application [~~results from~~]**is a continuation of** PCT application no. PCT/JP97/[~~04891~~]**04891**, filed on December 26, [~~1997~~]**1997**, claiming [~~a Convention~~]priority [~~from~~]**to** Japanese patent application no. 350152/[~~96~~]**96**, filed on December 27, [~~1996, and was filed with the U.S. Patent and Trademark Office for the national processing.~~]**1996.**

### IN THE CLAIMS

22. (Amended Twice) [~~A~~]**An** orthodontic [~~remedy~~]**method to increase tooth movement in a subject in need thereof,** comprising :

administering[~~, multiple times or~~] continuously[~~,~~] an amount of

**(A)** parathyroid hormone or [~~of~~]

**(B)** a parathyroid hormone derivative that has the same biological effect as full length parathyroid hormone[~~, that~~]**and is selected from the group consisting of:**

**(i) a peptide fragment of parathyroid hormone;**

**(ii) parathyroid hormone substituted at least one amino acid at positions 8, 18 or 34; and**

**(iii) a peptide fragment of parathyroid hormone substituted at least one amino acid at positions 8, 18 or 34.**

**wherein the administered parathyroid hormone or parathyroid hormone derivative results in an increase in tooth movement in [a subject in need thereof]said subject.**

44. (Amended Once) The method of claim [~~43~~]**22** [~~where~~]**wherein** said parathyroid hormone derivative is substituted parathyroid hormone from the group consisting of parathyroid hormone substituted at amino acid 8 with leucine or norleucine, parathyroid hormone substituted at amino acid 18 with leucine or norleucine, parathyroid hormone substituted at amino acid 34 with tyrosine.

45. (Amended Once) The method of claim ~~[43]~~22 ~~[where]~~wherein said parathyroid hormone derivative is a peptide fragment from the group consisting of human parathyroid hormone (1-34), (1-37), (1-38), and (1-64).

46. (Amended Once) The method of claim 45 ~~[where]~~wherein said peptide fragment is a substituted is a substituted peptide fragment from the group consisting of a peptide fragment substituted at amino acid 8 with leucine or norleucine, a peptide fragment substituted at amino acid 18 with leucine or norleucine, a peptide fragment substituted at amino acid 34 with tyrosine.